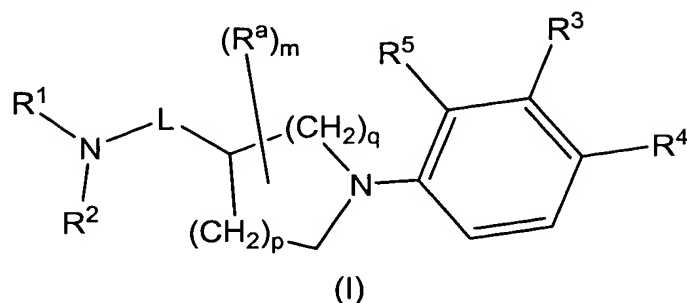


What is claimed is:

1. A composition comprising a compound of formula (I):



wherein

L is a direct bond, or an optionally C₁₋₄alkyl substituted radical selected from the group consisting of C₁₋₄alkylene or C₃₋₄alkenylene wherein NR¹R² is attached to an sp³ hybridized carbon, C₃₋₄alkynylene wherein NR¹R² is attached to an sp³ hybridized carbon, C₂₋₄alkylidene wherein NR¹R² is attached to an sp³ hybridized carbon, aryloxy wherein NR¹R² is not attached to the oxygen, arylthio wherein NR¹R² is not attached to the sulfur, C₂₋₄alkoxy wherein NR¹R² is not attached to the oxygen or a carbon attached to the oxygen, C₂₋₄alkylthio wherein NR¹R² is not attached to the sulfur or a carbon attached to the sulfur, and -C₂₋₃alkyl-X-C₁₋₂alkyl- wherein X is O, S or NH and wherein NR¹R² is not attached to a carbon attached to X;

p is 0, 1 or 2;

q is 1 or 2; provided that 2 ≤ p+q ≤ 4;

R¹ is a substituent independently selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₃₋₆ alkenyl, C₃₋₉ carbocyclyl, 3-12 membered heterocyclyl, phenyl, (5-9-membered heterocyclyl)C₁₋₆ alkylene, and (phenyl)C₁₋₆ alkylene;

R² is a substituent independently selected from the group consisting of C₁₋₆ alkyl, C₃₋₆ alkenyl, C₃₋₉ membered carbocyclyl, 3-12 membered heterocyclyl, phenyl, (5-9-membered heterocyclyl)C₁₋₆ alkylene, and (phenyl)C₁₋₆ alkylene;

or R¹ and R² taken together with the nitrogen to which they are attached
 form a saturated 3-13 membered N-linked heterocyclyl, wherein,
 in addition to the N-linking nitrogen, the 3-13 membered
 heterocyclyl may optionally contain between 1 and 3 additional
 5 heteroatoms independently selected from O, S, and NH;
 wherein R¹ and R² are optionally and independently substituted with 1-3
 substituents selected from the group consisting of *tert*-
 butyloxycarbonyl, hydroxy, halo, nitro, amino, cyano,
 carboxamide, C₁₋₆ alkyl, C₁₋₆ acyl, 5-9-membered heterocyclyl,
 10 -N(C₁₋₆ alkyl)(5-9 membered heterocyclyl), -NH(5-9 membered
 heterocyclyl), -O(5-9 membered heterocyclyl), (5-9 membered
 heterocyclyl)C₁₋₃ alkylene, C₁₋₂-hydroxyalkylene, C₁₋₆ alkoxy, (C₃₋₆
 cycloalkyl)-O-, phenyl, (phenyl)C₁₋₃ alkylene, and (phenyl)C₁₋₃
 alkylene-O-; and wherein each of the preceding substituents of
 15 R¹ and R² may optionally have between 1 and 3 substituents
 independently selected from the group consisting of
 trifluoromethyl, halo, nitro, cyano, hydroxy, and C₁₋₃ alkyl;
 one of R³, R⁴ and R⁵ is G and the other two independently are
 hydrogen, fluoro, chloro, bromo, nitro, trifluoromethyl, methyl, or
 20 C₁₋₃ alkoxy ;
 G is L²Q;
 L² is unbranched -(CH₂)_n- wherein n is an integer from 1 to 7;
 Q is NR⁸R⁹ wherein R⁸ is independently selected from hydrogen, C₁₋₆
 alkyl, C₃₋₆ alkenyl, C₃₋₉ carbocyclyl, 3-12 membered heterocyclyl,
 25 phenyl, (5-9-membered heterocyclyl)C₁₋₆ alkylene, and
 (phenyl)C₁₋₆ alkylene; and R⁹ is independently selected from C₁₋₆
 alkyl, C₃₋₆ alkenyl, 3-9 membered carbocyclyl, 3-13 membered
 heterocyclyl, phenyl, (5-9-membered heterocyclyl)C₁₋₆ alkylene,
 and (phenyl)C₁₋₆ alkylene; or Q is a saturated 3-15 membered N-
 30 linked heterocyclyl, wherein, in addition to the N-linking nitrogen,
 the 3-15 membered heterocyclyl may optionally contain between
 1 and 4 additional heteroatoms independently selected from O,
 S, and NH;

wherein Q is optionally substituted with 1-3 substituents selected (in addition to the preceding paragraph) from the group consisting of *tert*-butoxycarbonyl, hydroxy, halo, nitro, amino, cyano, carboxamide, C₁₋₆ alkyl, C₁₋₆ acyl, 5-9-membered heterocyclyl, -N(C₁₋₆ alkyl)(5-9 membered heterocyclyl), -NH(5-9 membered heterocyclyl), -O(5-9 membered heterocyclyl), (5-9 membered heterocyclyl)C₁₋₃ alkylene, C₁₋₂-hydroxyalkylene, C₁₋₆ alkoxy, (C₃₋₆ cycloalkyl)-O-, phenyl, (phenyl)C₁₋₃ alkylene, and (phenyl)C₁₋₃ alkylene-O-; and where said substituent groups of Q may optionally have between 1 and 3 substituents independently selected from trifluoromethyl, halo, nitro, cyano, hydroxy, and C₁₋₃ alkyl;

R^a are independently C₁₋₃ alkyl, trifluoromethyl;

m is 0, 1, 2 or 3; and

wherein each of the above alkyl, alkylene, alkenyl, heterocyclyl, cycloalkyl, carbocyclyl, and aryl groups may each be independently and optionally substituted with between 1 and 3 substituents independently selected from methoxy, halo, amino, nitro, hydroxy, and C₁₋₃ alkyl; or a pharmaceutically acceptable salt, ester, tautomer, solvate or amide thereof.

2. A compound of claim 1, wherein NR¹R² taken together form substituted or unsubstituted morpholinyl, thiomorpholinyl, piperidinyl, methylpiperidinyl, piperazinyl, N-methylpiperazinyl, dimethylamino, pyrrolidinyl, azatricyclodecanyl, cyclohexylmethylamino, methylphenethylamino, pyridylamino, anilino, diethylamino, methylethylamino, ethylpropylamino, or dipropylamino;
3. A compound of claim 1, wherein NR¹R² taken together form a saturated N-linked nitrogen-containing heterocyclyl.

4. A compound of claim 1, wherein NR^1R^2 taken together form a substituent selected from substituted or unsubstituted piperidinyl, substituted or unsubstituted piperazinyl, pyrrolinyl, pyrrolidinyl, thiomorpholinyl, and morpholinyl.
5. A compound of claim 1, wherein wherein NR^1R^2 taken together form a substituent selected from N-(C₁₋₆ alkyl)piperazinyl, N-phenyl-piperazinyl, 1,3,8-triaza-spiro{4.5}decyl, and 1,4-dioxa-8-aza-spiro{4.5}decyl.
6. A compound of claim 2, wherein NR^1R^2 taken together form a monovalent radical of an amine selected from the group consisting of aziridine, 1,4,7-trioxa-10-aza-cyclododecane, thiazolidine, 1-phenyl-1,3,8-triaza-spiro{4.5}decan-4-one, piperidine-3-carboxylic acid diethylamide, 1,2,3,4,5,6-hexahydro-{2,3'}bipyridinyl, 4-(3-trifluoromethyl-phenyl)-piperazine, 2-piperazin-1-yl-pyrimidine, piperidine-4-carboxylic acid amide, methyl-(2-pyridin-2-yl-ethyl)-amine, {2-(3,4-dimethoxy-phenyl)-ethyl}-methyl-amine, thiomorpholinyl, allyl-cyclopentyl-amine, {2-(1H-indol-3-yl)-ethyl}-methyl-amine, 1-piperidin-4-yl-1,3-dihydro-benzoimidazol-2-one, 2-(piperidin-4-yloxy)-pyrimidine, piperidin-4-yl-pyridin-2-yl-amine, phenylamine, pyridin-2-ylamine.
7. A compound of claim 4, wherein NR^1R^2 taken together form a substituent selected from the group consisting of morpholinyl and piperidinyl, wherein said substituent is optionally substituted with between 1 and 3 substituents selected from hydroxy, halo, carboxamide, C₁₋₆ alkyl, C₁₋₆ acyl, 5-9 membered heterocyclyl, -N(C₁₋₆ alkyl)(5-9 membered heterocyclyl), -NH(5-9 membered heterocyclyl), -O(5-9 membered heterocyclyl), (5-9 membered heterocyclyl)C₁₋₃ alkylene, C₁₋₂-hydroxyalkylene, C₁₋₆ alkoxy, (C₃₋₆ cycloalkyl)-O-, phenyl, (phenyl)C₁₋₃ alkylene, and (phenyl)C₁₋₃ alkylene-O- where each of above heterocyclyl, phenyl, and alkyl groups may be optionally substituted with from 1 to 3 substituents independently selected from trifluoromethyl, halo, nitro, cyano, hydroxy, and C₁₋₃ alkyl.

8. A compound of claim 3, wherein the saturated N-linked nitrogen-containing heterocyclyl is substituted with a substituent selected from the group consisting of pyridyl, pyrimidyl, furyl, thiofuryl, imidazolyl, (imidazolyl)C₁₋₆ alkylene, oxazolyl, thiazolyl, 2,3-dihydro-indolyl, benzimidazolyl, 2-oxobenzimidazolyl, (tetrazolyl)C₁₋₆ alkylene, tetrazolyl, (triazolyl)C₁₋₆ alkylene, triazolyl, (pyrrolyl)C₁₋₆ alkylene, pyrrolidinyl, and pyrrolyl.
9. A compound of claim 1, wherein NR¹R² taken together form morpholinyl, piperidinyl, pyrrolidinyl, or diethylamino.
10. A compound of claim 1, wherein Q is morpholinyl, piperidinyl, pyrrolidinyl, or diethylamino.
11. A compound of claim 1, wherein NR¹R² taken together form morpholinyl, piperidinyl, or pyrrolidinyl.
12. A compound of claim 1, wherein Q is morpholinyl, piperidinyl, or pyrrolidinyl.
13. A compound of claim 12, wherein NR¹R² is a substituted or unsubstituted morpholino.
14. A compound of claim 1, wherein one of R³ and R⁴ is G.
15. A compound of claim 1, wherein R⁴ is G.
16. A compound of claim 14, wherein R³ is G.
17. A compound of claim 1, wherein q is 2 and p is 1.
18. A compound of claim 1, wherein q is 1 and p is 1.

19. A compound of claim 1, wherein q is 2 and p is 2.
20. A compound of claim 1, wherein L is -CH₂-.
- 5 21. A compound of claim 1, wherein L is a direct bond.
22. A compound of claim 1, wherein L is -CH₂CH₂-.
- 10 23. A compound of claim 1, wherein L² is -CH₂-
24. A compound of claim 1, wherein Q is selected from the group consisting of substituted or unsubstituted pyrrolidinyl, piperidinyl, methylpiperidinyl, morpholinyl, thiomorpholinyl, azatricyclodecanyl, cyclohexylamino, cyclohexylmethylamino, piperazinyl, N-methylpiperazinyl, dimethylamino, methylphenethylamino, pyridylamino, anilino, diethylamino, methylethylamino, ethylpropylamino, dipropylamino, or 1,4,7,10-tetraoxa-13-aza-cyclopentadecanyl.
- 15
- 20 25. A compound of claim 1, wherein Q is a saturated N-linked nitrogen-containing heterocyclyl.
26. A compound of claim 1, wherein Q is a substituent selected from the group consisting of substituted piperidinyl, unsubstituted piperidinyl, substituted piperazinyl, unsubstituted piperazinyl, pyrrolinyl, pyrrolidinyl, thiomorpholinyl, and morpholinyl.
- 25
27. A compound of claim 1, wherein substituted Q is N-(C₁₋₆ alkyl)piperazinyl, N-phenyl-piperazinyl, 1,3,8-triaza-spiro{4.5}decyl, or 1,4-dioxa-8-aza-spiro{4.5}decyl.
- 30
28. A compound of claim 25, wherein Q is a monovalent radical of an amine selected from the group consisting of aziridine, 1,4,7-trioxa-10-aza-

cyclododecane, thiazolidine, 1-phenyl-1,3,8-triaza-spiro{4.5}decan-4-one, piperidine-3-carboxylic acid diethylamide, 1,2,3,4,5,6-hexahydro-{2,3'}bipyridinyl, 4-(3-trifluoromethyl-phenyl)-piperazine, 2-piperazin-1-yl-pyrimidine, piperidine-4-carboxylic acid amide, methyl-(2-pyridin-2-yl-ethyl)-amine, {2-(3,4-dimethoxy-phenyl)-ethyl}-methyl-amine, thiomorpholinyl, allyl-cyclopentyl-amine, {2-(1H-indol-3-yl)-ethyl}-methyl-amine, 1-piperidin-4-yl-1,3-dihydro-benzoimidazol-2-one, 2-(piperidin-4-yloxy)-pyrimidine, piperidin-4-yl-pyridin-2-yl-amine, phenylamine, and pyridin-2-ylamine.

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29. A compound of claim 25, wherein Q is morpholinyl, pyridyl, or piperidinyl, and wherein Q is optionally substituted with between 1 and 3 substituents selected from hydroxy, halo, carboxamide, C₁₋₆ alkyl, C₁₋₆ acyl, 5-9 membered or 6-9 membered heterocyclyl, -N(C₁₋₆ alkyl)(5-9 membered or 6-9 membered heterocyclyl), -NH(5-9 membered or 6-9 membered heterocyclyl), -O(5-9 or 6-9 membered heterocyclyl), (5-9 membered or 6-9 membered heterocyclyl)C₁₋₃ alkylene, C₁₋₂-hydroxyalkylene, C₁₋₆ alkoxy, (C₃₋₆ cycloalkyl)-O-, phenyl, (phenyl)C₁₋₃ alkylene, and (phenyl)C₁₋₃ alkylene-O- where each of above heterocyclyl, phenyl, and alkyl groups may be optionally substituted with from 1 to 3 substituents independently selected from trifluoromethyl, halo, nitro, cyano, hydroxy, and C₁₋₃ alkyl.

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30. A compound of claim 29, wherein Q is substituted with a substituent comprising a 5-9 membered heterocyclyl group selected from: pyridyl, pyrimidyl, furyl, thiofuryl, imidazolyl, (imidazolyl)C₁₋₆ alkylene, oxazolyl, thiazolyl, 2,3-dihydro-indolyl, benzimidazolyl, 2-oxobenzimidazolyl, (tetrazolyl)C₁₋₆ alkylene, tetrazolyl, (triazolyl)C₁₋₆ alkylene, triazolyl, (pyrrolyl)C₁₋₆ alkylene, pyrrolidinyl, and pyrrolyl.

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31. A compound of claim 30, wherein Q is a substituted or unsubstituted morpholinyl.

- 32 A compound of claim 1, wherein R⁸ is hydrogen.
33. A compound of claim 1, wherein R⁸ is C₁₋₆ alkyl.
- 5 34. A compound of claim 1, wherein R⁸ is cyclohexyl.
35. A compound of claim 1, wherein R⁸ and R⁹ independently are C₁₋₆ alkyl.
36. A compound of claim 1, wherein R⁸ and R⁹ are methyl.
- 10 37. A compound of claim 1, wherein R⁸ and R⁹ are ethyl.
38. A compound of claim 32, wherein R⁹ is selected from phenyl or 5-9
membered aromatic heterocyclyl, wherein said phenyl or aromatic
15 heterocyclyl is optionally substituted with 1-3 substituents selected from
hydroxy, halo, nitro, cyano, trifluoromethyl, and C₁₋₃ alkyl.
39. A compound of claim 38, wherein R⁹ is selected from substituted or
unsubstituted phenyl, pyridyl, pyrimidyl, furyl, thiofuryl, imidazolyl,
20 (imidazolyl)C₁₋₆ alkylene, oxazolyl, thiazolyl, 2,3-dihydro-indolyl,
benzimidazolyl, 2-oxobenzimidazolyl, (tetrazolyl)C₁₋₆ alkylene, tetrazolyl,
(triazolyl)C₁₋₆ alkylene, triazolyl, (pyrrolyl)C₁₋₆ alkylene, and pyrrolyl.
40. A compound of claim 39, wherein R⁹ is substituted or unsubstituted
25 phenyl.
41. A compound of claim 39, wherein R⁹ is substituted or unsubstituted
pyridyl.
- 30 42. A compound of claim 1, wherein:
R¹ and R² are independently selected from C₂ alkyl, or taken together
with the nitrogen to which they are attached, they form a non-

aromatic 5-6 membered heterocyclyl optionally including an additional heteroatom independently selected from O, S, and NH; one of R³, R⁴, and R⁵ is G and the two remaining are H;

G is L²Q;

5 L² is methylene;

Q is NR⁸R⁹ wherein R⁸ is independently selected from hydrogen, C₁₋₂ alkyl, C₃ alkenyl, C₅₋₉ carbocyclyl, 3-12 membered heterocyclyl, phenyl, (5-9-membered heterocyclyl)C₁₋₆ alkylene, and (phenyl)C₁₋₆ alkylene; and R⁹ is independently selected from C₁₋₂ alkyl, C₃ alkenyl, C₅₋₉ carbocyclyl, 3-12 membered heterocyclyl, phenyl, (6-9-membered heterocyclyl)C₁₋₆ alkylene, and (phenyl)C₁₋₆ alkylene; or Q is a saturated 3-15 membered N-linked heterocyclyl, wherein, in addition to the N-linking nitrogen, the 3-15 membered heterocyclyl may optionally contain between 1 and 4 additional heteroatoms selected from O, S, and NH;

wherein each of the above alkyl, alkylene, alkenyl, alkenylene, heterocyclyl, and carbocyclyl groups may each be independently and optionally substituted with between 1 and 3 substituents selected from methoxy, halo, amino, nitro, hydroxyl, and C₁₋₃ alkyl;

wherein substituents of Q can be further selected from *tert*-butyloxycarbonyl, hydroxy, halo, nitro, amino, cyano, carboxamide, 5-9-membered heterocyclyl, -NH(6-membered heterocyclyl), -O(6-membered heterocyclyl), C₂-hydroxyalkylene, phenyl, benzyl and, where each of above heterocyclyl, phenyl, and alkyl substituent groups of Q may be optionally substituted with trifluoromethyl;

or a pharmaceutically acceptable salt, ester, tautomer, solvate or amide thereof.

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43. A compound of claim 1, wherein NR¹R² taken together form morpholinyl, piperidinyl, pyrrolidinyl, or diethylamino,

p is 1 and q is 2, and

Q is selected from substituted or unsubstituted piperidinyl, piperazinyl, pyrrolinyl, pyrrolidinyl, thiomorpholinyl, and morpholinyl.

- 5 44. A compound of claim 1, wherein (a) NR^1R^2 taken together form piperidinyl or pyrrolidinyl, (b) n is 1, (c) p is 1 and q is 2, and (d) Q is selected from morpholinyl and piperidinyl.
- 10 45. A compound of claim 1, wherein (a) NR^1R^2 taken together form piperidinyl or pyrrolidinyl, (b) n is 1, (c) p is 1 and q is 2, and (d) Q is selected from morpholinyl and piperidinyl.
- 15 46. A compound of claim 44, wherein Q is piperidinyl or substituted piperidinyl.
- 20 47. A compound of claim 1, wherein NR^1R^2 taken together form piperidinyl, pyrrolidinyl, or diethylamino, n is 1, p is 1 and q is 2, and Q is NR^8R^9 and R^8 is H and R^9 is selected from phenyl or aromatic 5-9 membered heterocyclyl, wherein said phenyl or heterocyclyl is optionally substituted with 1-3 substituents selected from trifluoromethyl, halo, nitro, cyano, hydroxy, and C_{1-3} alkyl.
- 25 48. A compound of claim 1 wherein R^a is hydrogen.
- 30 49. A compound of claim 1 selected from the group consisting of 4-{2-(4-Piperidin-1-ylmethyl-piperidin-1-yl)-benzyl}-morpholine; Cyclohexyl-{1-(4-pyrrolidin-1-ylmethyl-phenyl)-piperidin-4-ylmethyl}-amine; 1-{1-(4-Pyrrolidin-1-ylmethyl-phenyl)-piperidin-4-ylmethyl}-azacyclotridecane; Diethyl-{1-(4-pyrrolidin-1-ylmethyl-phenyl)-piperidin-4-ylmethyl}-amine;

Dimethyl-{1-(4-pyrrolidin-1-ylmethyl-phenyl)-piperidin-4-ylmethyl}-amine;
 1-Methyl-4-{1-(4-pyrrolidin-1-ylmethyl-phenyl)-piperidin-4-ylmethyl}-
 piperazine;
 1-{1-(4-Pyrrolidin-1-ylmethyl-phenyl)-piperidin-4-ylmethyl}-piperidin-4-ol;
 5 4-{1-(4-Pyrrolidin-1-ylmethyl-phenyl)-piperidin-4-ylmethyl}-
 thiomorpholine;
 1-{1-(4-Pyrrolidin-1-ylmethyl-phenyl)-piperidin-4-ylmethyl}-piperidine;
 4-{1-(4-Pyrrolidin-1-ylmethyl-phenyl)-piperidin-4-ylmethyl}-morpholine;
 4-{3-(4-Pyrrolidin-1-ylmethyl-piperidin-1-yl)-benzyl}-thiomorpholine;
 10 4-{3-(4-Pyrrolidin-1-ylmethyl-piperidin-1-yl)-benzyl}-morpholine;
 4-Pyrrolidin-1-ylmethyl-1-(3-pyrrolidin-1-ylmethyl-phenyl)-piperidine;
 1-{3-(4-Pyrrolidin-1-ylmethyl-piperidin-1-yl)-benzyl}-piperidine;
 1-{4-(4-Pyrrolidin-1-ylmethyl-piperidin-1-yl)-benzyl}-azacyclotridecane;
 Cyclohexyl-{4-(4-pyrrolidin-1-ylmethyl-piperidin-1-yl)-benzyl}-amine;
 15 1-{4-(4-Pyrrolidin-1-ylmethyl-piperidin-1-yl)-benzyl}-piperidin-4-ol;
 1-Methyl-4-{4-(4-pyrrolidin-1-ylmethyl-piperidin-1-yl)-benzyl}-piperazine;
 4-{4-(4-Pyrrolidin-1-ylmethyl-piperidin-1-yl)-benzyl}-thiomorpholine;
 4-{4-(4-Pyrrolidin-1-ylmethyl-piperidin-1-yl)-benzyl}-morpholine;
 Dimethyl-{4-(4-pyrrolidin-1-ylmethyl-piperidin-1-yl)-benzyl}-amine;
 20 4-{2-(4-Pyrrolidin-1-ylmethyl-piperidin-1-yl)-benzyl}-morpholine;
 4-{1-(4-Piperidin-1-ylmethyl-phenyl)-piperidin-4-ylmethyl}-morpholine;
 1-{4-(4-Pyrrolidin-1-ylmethyl-piperidin-1-yl)-benzyl}-piperidine;
 Cyclohexyl-{1-(4-morpholin-4-ylmethyl-phenyl)-piperidin-4-yl}-amine;
 Cyclohexyl-methyl-{1-(4-morpholin-4-ylmethyl-phenyl)-piperidin-4-yl}-
 25 amine;
 4-{4-{4-(4-Methyl-piperazin-1-yl)-piperidin-1-yl}-benzyl}-morpholine;
 Ethyl-methyl-{1-(4-morpholin-4-ylmethyl-phenyl)-piperidin-4-yl}-amine;
 4-{1-(4-Morpholin-4-ylmethyl-phenyl)-piperidin-4-yl}-morpholine;
 4-{4-(4-Pyrrolidin-1-yl-piperidin-1-yl)-benzyl}-morpholine;
 30 1'-(4-Morpholin-4-ylmethyl-phenyl)-{1,4'}bipiperidinyl;
 1'-(4-Piperidin-1-ylmethyl-phenyl)-{1,4'}bipiperidinyl;
 (4-{1,4'}Bipiperidinyl-1'-yl-benzyl)-pyridin-2-yl-amine;
 Phenyl-{1-(4-pyrrolidin-1-ylmethyl-phenyl)-piperidin-4-ylmethyl}-amine;

Pyridin-2-yl-{1-(4-pyrrolidin-1-ylmethyl-phenyl)-piperidin-4-ylmethyl}-
amine;

1-{1-(4-Piperidin-1-ylmethyl-phenyl)-piperidin-4-ylmethyl}-piperidine;

4-Pyrrolidin-1-ylmethyl-1-(4-pyrrolidin-1-ylmethyl-phenyl)-piperidine;

5 (4-Fluoro-phenyl)-{4-(4-pyrrolidin-1-ylmethyl-piperidin-1-yl)-benzyl}-
amine;

4-{2-{1-(4-Piperidin-1-ylmethyl-phenyl)-pyrrolidin-3-yl}-ethyl}-morpholine;

Diethyl-{2-{1-(4-piperidin-1-ylmethyl-phenyl)-pyrrolidin-3-yl}-ethyl}-amine;

Methyl-phenethyl-{2-{1-(4-piperidin-1-ylmethyl-phenyl)-pyrrolidin-3-yl}-
ethyl}-amine;

10 ethyl}-amine;

1-[4-(4-Pyrrolidin-1-ylmethyl-piperidin-1-yl)-3-trifluoromethyl-benzyl]-
piperidine;

1-(2-Nitro-4-pyrrolidin-1-ylmethyl-phenyl)-4-pyrrolidin-1-ylmethyl-
piperidine;

15 4-[3-Nitro-4-(4-pyrrolidin-1-ylmethyl-piperidin-1-yl)-benzyl]-morpholine;

1-[3-Nitro-4-(4-pyrrolidin-1-ylmethyl-piperidin-1-yl)-benzyl]-piperidin-4-ol;

1-[4-(4-Pyrrolidin-1-ylmethyl-piperidin-1-yl)-2-trifluoromethyl-benzyl]-
piperidine;

1-Isopropyl-4-[3-methyl-4-(4-pyrrolidin-1-ylmethyl-piperidin-1-yl)-benzyl]-
20 piperazine;

1-(2-Methyl-4-pyrrolidin-1-ylmethyl-phenyl)-4-pyrrolidin-1-ylmethyl-
pyrrolidine;

1-[3-Methyl-4-(4-pyrrolidin-1-ylmethyl-piperidin-1-yl)-benzyl]-pyrrolidine;

1-{1-[4-(4-Pyrrolidin-1-yl-piperidin-1-ylmethyl)-2-trifluoromethyl-phenyl]-
25 piperidin-4-ylmethyl}-pyrrolidine;

1-(1-{3-Trifluoromethyl-4-[4-(4-trifluoromethyl-phenyl)-piperidin-1-
ylmethyl]-phenyl}-piperidin-4-ylmethyl)-pyrrolidine;

1-{1-[2-Fluoro-4-(4-phenyl-piperidin-1-ylmethyl)-phenyl]-piperidin-4-
ylmethyl}-pyrrolidine;

30 [3-Fluoro-4-(4-pyrrolidin-1-ylmethyl-piperidin-1-yl)-benzyl]-dimethyl-
amine;

1-[3-Fluoro-4-(4-pyrrolidin-1-ylmethyl-piperidin-1-yl)-benzyl]-piperidine;

13-[4-(4-Pyrrolidin-1-ylmethyl-piperidin-1-yl)-2-trifluoromethyl-benzyl]-
 1,4,7,10-tetraoxa-13-aza-cyclopentadecane
 ditrifluoromethanesulfonate; and
 {1-[4-(4-Pyrrolidin-1-ylmethyl-piperidin-1-yl)-3-trifluoromethyl-benzyl]-
 5 piperidin-4-yl}-methanol.

50. A compound of claim 1 selected from the group consisting of
 (4-{1,4'}Bipiperidinyl-1'-yl-benzyl)-pyridin-2-yl-amine;
 1'-(4-Morpholin-4-ylmethyl-phenyl)-{1,4'}bipiperidinyl;
 10 1'-(4-Piperidin-1-ylmethyl-phenyl)-{1,4'}bipiperidinyl;
 1-{1-(4-Piperidin-1-ylmethyl-phenyl)-piperidin-4-ylmethyl}-piperidine;
 4-{1-(4-Piperidin-1-ylmethyl-phenyl)-piperidin-4-ylmethyl}-morpholine;
 1-{1-(4-Pyrrolidin-1-ylmethyl-phenyl)-piperidin-4-ylmethyl}-piperidin-4-ol;
 1-{1-(4-Pyrrolidin-1-ylmethyl-phenyl)-piperidin-4-ylmethyl}-piperidine;
 15 1-{3-(4-Pyrrolidin-1-ylmethyl-piperidin-1-yl)-benzyl}-piperidine;
 1-{4-(4-Pyrrolidin-1-ylmethyl-piperidin-1-yl)-benzyl}-azacyclotridecane;
 1-{4-(4-Pyrrolidin-1-ylmethyl-piperidin-1-yl)-benzyl}-piperidin-4-ol;
 1-{4-(4-Pyrrolidin-1-ylmethyl-piperidin-1-yl)-benzyl}-piperidine;
 1-Methyl-4-{1-(4-pyrrolidin-1-ylmethyl-phenyl)-piperidin-4-ylmethyl}-
 20 piperazine;
 1-Methyl-4-{4-(4-pyrrolidin-1-ylmethyl-piperidin-1-yl)-benzyl}-piperazine;
 4-{1-(4-Pyrrolidin-1-ylmethyl-phenyl)-piperidin-4-ylmethyl}-morpholine;
 4-{1-(4-Pyrrolidin-1-ylmethyl-phenyl)-piperidin-4-ylmethyl}-
 thiomorpholine;
 25 4-{3-(4-Pyrrolidin-1-ylmethyl-piperidin-1-yl)-benzyl}-thiomorpholine;
 4-{4-(4-Pyrrolidin-1-ylmethyl-piperidin-1-yl)-benzyl}-thiomorpholine;
 4-{2-{1-(4-Piperidin-1-ylmethyl-phenyl)-pyrrolidin-3-yl}-ethyl}-morpholine;
 4-Pyrrolidin-1-ylmethyl-1-(3-pyrrolidin-1-ylmethyl-phenyl)-piperidine;
 4-Pyrrolidin-1-ylmethyl-1-(4-pyrrolidin-1-ylmethyl-phenyl)-piperidine;
 30 Cyclohexyl-{1-(4-pyrrolidin-1-ylmethyl-phenyl)-piperidin-4-ylmethyl}-
 amine;
 Cyclohexyl-{4-(4-pyrrolidin-1-ylmethyl-piperidin-1-yl)-benzyl}-amine;

- Cyclohexyl-methyl-{1-(4-morpholin-4-ylmethyl-phenyl)-piperidin-4-yl}-amine;
- Diethyl-{1-(4-pyrrolidin-1-ylmethyl-phenyl)-piperidin-4-ylmethyl}-amine;
- Diethyl-{2-{1-(4-piperidin-1-ylmethyl-phenyl)-pyrrolidin-3-yl}-ethyl}-amine;
- 5 Dimethyl-{1-(4-pyrrolidin-1-ylmethyl-phenyl)-piperidin-4-ylmethyl}-amine;
- Dimethyl-{4-(4-pyrrolidin-1-ylmethyl-piperidin-1-yl)-benzyl}-amine;
- Methyl-phenethyl-{2-{1-(4-piperidin-1-ylmethyl-phenyl)-pyrrolidin-3-yl}-ethyl}-amine;
- Phenyl-{1-(4-pyrrolidin-1-ylmethyl-phenyl)-piperidin-4-ylmethyl}-amine;
- 10 Pyridin-2-yl-{1-(4-pyrrolidin-1-ylmethyl-phenyl)-piperidin-4-ylmethyl}-amine;
- 1-(2-Nitro-4-pyrrolidin-1-ylmethyl-phenyl)-4-pyrrolidin-1-ylmethyl-piperidine;
- 1-[3-Nitro-4-(4-pyrrolidin-1-ylmethyl-piperidin-1-yl)-benzyl]-piperidin-4-ol;
- 15 1-[4-(4-Pyrrolidin-1-ylmethyl-piperidin-1-yl)-2-trifluoromethyl-benzyl]-piperidine;
- 1-(2-Methyl-4-pyrrolidin-1-ylmethyl-phenyl)-4-pyrrolidin-1-ylmethyl-pyrrolidine;
- 1-[3-Methyl-4-(4-pyrrolidin-1-ylmethyl-piperidin-1-yl)-benzyl]-pyrrolidine;
- 20 1-{1-[4-(4-Pyrrolidin-1-yl-piperidin-1-ylmethyl)-2-trifluoromethyl-phenyl]-piperidin-4-ylmethyl}-pyrrolidine;
- 1-{1-[2-Fluoro-4-(4-phenyl-piperidin-1-ylmethyl)-phenyl]-piperidin-4-ylmethyl}-pyrrolidine;
- [3-Fluoro-4-(4-pyrrolidin-1-ylmethyl-piperidin-1-yl)-benzyl]-dimethyl-
- 25 amine; and
- 1-[3-Fluoro-4-(4-pyrrolidin-1-ylmethyl-piperidin-1-yl)-benzyl]-piperidine.
51. A compound of claim 1 selected from the group consisting of
- 1'-(4-Piperidin-1-ylmethyl-phenyl)-{1,4'}bipiperidinyI;
- 30 1-{1-(4-Piperidin-1-ylmethyl-phenyl)-piperidin-4-ylmethyl}-piperidine;
- 4-{1-(4-Piperidin-1-ylmethyl-phenyl)-piperidin-4-ylmethyl}-morpholine;
- 1-{1-(4-Pyrrolidin-1-ylmethyl-phenyl)-piperidin-4-ylmethyl}-piperidin-4-ol;
- 1-{1-(4-Pyrrolidin-1-ylmethyl-phenyl)-piperidin-4-ylmethyl}-piperidine;

- 1-{4-(4-Pyrrolidin-1-ylmethyl-piperidin-1-yl)-benzyl}-piperidin-4-ol;
 1-{4-(4-Pyrrolidin-1-ylmethyl-piperidin-1-yl)-benzyl}-piperidine;
 1-Methyl-4-{1-(4-pyrrolidin-1-ylmethyl-phenyl)-piperidin-4-ylmethyl}-
 piperazine;
 5 4-{1-(4-Pyrrolidin-1-ylmethyl-phenyl)-piperidin-4-ylmethyl}-morpholine;
 4-{1-(4-Pyrrolidin-1-ylmethyl-phenyl)-piperidin-4-ylmethyl}-
 thiomorpholine;
 4-{4-(4-Pyrrolidin-1-ylmethyl-piperidin-1-yl)-benzyl}-thiomorpholine;
 4-{2-{1-(4-Piperidin-1-ylmethyl-phenyl)-pyrrolidin-3-yl}-ethyl}-morpholine;
 10 4-Pyrrolidin-1-ylmethyl-1-(4-pyrrolidin-1-ylmethyl-phenyl)-piperidine;
 Cyclohexyl-{1-(4-pyrrolidin-1-ylmethyl-phenyl)-piperidin-4-ylmethyl}-
 amine;
 Cyclohexyl-{4-(4-pyrrolidin-1-ylmethyl-piperidin-1-yl)-benzyl}-amine;
 Diethyl-{1-(4-pyrrolidin-1-ylmethyl-phenyl)-piperidin-4-ylmethyl}-amine;
 15 Diethyl-{2-{1-(4-piperidin-1-ylmethyl-phenyl)-pyrrolidin-3-yl}-ethyl}-amine;
 Dimethyl-{1-(4-pyrrolidin-1-ylmethyl-phenyl)-piperidin-4-ylmethyl}-amine;
 Dimethyl-{4-(4-pyrrolidin-1-ylmethyl-piperidin-1-yl)-benzyl}-amine;
 Methyl-phenethyl-{2-{1-(4-piperidin-1-ylmethyl-phenyl)-pyrrolidin-3-yl}-
 ethyl}-amine;
 20 Pyridin-2-yl-{1-(4-pyrrolidin-1-ylmethyl-phenyl)-piperidin-4-ylmethyl}-
 amine;
 1-(2-Nitro-4-pyrrolidin-1-ylmethyl-phenyl)-4-pyrrolidin-1-ylmethyl-
 piperidine;
 1-[3-Nitro-4-(4-pyrrolidin-1-ylmethyl-piperidin-1-yl)-benzyl]-piperidin-4-ol;
 25 1-(2-Methyl-4-pyrrolidin-1-ylmethyl-phenyl)-4-pyrrolidin-1-ylmethyl-
 pyrrolidine;
 [3-Fluoro-4-(4-pyrrolidin-1-ylmethyl-piperidin-1-yl)-benzyl]-dimethyl-
 amine; and
 1-[3-Fluoro-4-(4-pyrrolidin-1-ylmethyl-piperidin-1-yl)-benzyl]-piperidine.
 30
52. A compound of claim 1 selected from the group consisting of
 1-{1-(4-Pyrrolidin-1-ylmethyl-phenyl)-piperidin-4-ylmethyl}-piperidin-4-ol;
 1-{1-(4-Pyrrolidin-1-ylmethyl-phenyl)-piperidin-4-ylmethyl}-piperidine;

1-Methyl-4-{1-(4-pyrrolidin-1-ylmethyl-phenyl)-piperidin-4-ylmethyl}-
piperazine;
1-{4-(4-Pyrrolidin-1-ylmethyl-piperidin-1-yl)-benzyl}-piperidine;
4-{1-(4-Pyrrolidin-1-ylmethyl-phenyl)-piperidin-4-ylmethyl}-morpholine;
5 4-{1-(4-Pyrrolidin-1-ylmethyl-phenyl)-piperidin-4-ylmethyl}-
thiomorpholine;
4-{2-{1-(4-Piperidin-1-ylmethyl-phenyl)-pyrrolidin-3-yl}-ethyl}-morpholine;
4-Pyrrolidin-1-ylmethyl-1-(4-pyrrolidin-1-ylmethyl-phenyl)-piperidine;
Cyclohexyl-{1-(4-pyrrolidin-1-ylmethyl-phenyl)-piperidin-4-ylmethyl}-
10 amine;
Cyclohexyl-{4-(4-pyrrolidin-1-ylmethyl-piperidin-1-yl)-benzyl}-amine;
Diethyl-{1-(4-pyrrolidin-1-ylmethyl-phenyl)-piperidin-4-ylmethyl}-amine;
Diethyl-{2-{1-(4-piperidin-1-ylmethyl-phenyl)-pyrrolidin-3-yl}-ethyl}-amine;
Dimethyl-{1-(4-pyrrolidin-1-ylmethyl-phenyl)-piperidin-4-ylmethyl}-amine;
15 Methyl-phenethyl-{2-{1-(4-piperidin-1-ylmethyl-phenyl)-pyrrolidin-3-yl}-
ethyl}-amine;
1-(2-Nitro-4-pyrrolidin-1-ylmethyl-phenyl)-4-pyrrolidin-1-ylmethyl-
piperidine; and
1-(2-Methyl-4-pyrrolidin-1-ylmethyl-phenyl)-4-pyrrolidin-1-ylmethyl-
20 pyrrolidine.

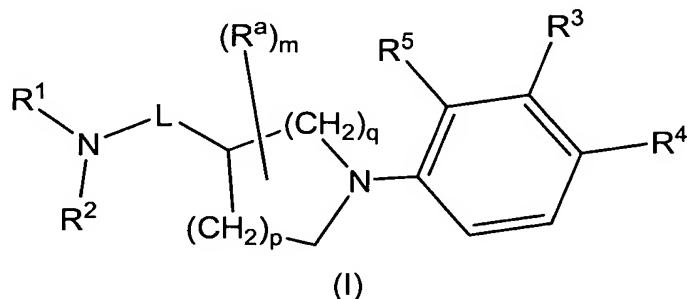
53. A compound of claim 1 selected from the group consisting of
1-{1-(4-Pyrrolidin-1-ylmethyl-phenyl)-piperidin-4-ylmethyl}-piperidin-4-ol;
1-{1-(4-Pyrrolidin-1-ylmethyl-phenyl)-piperidin-4-ylmethyl}-piperidine;
25 4-Pyrrolidin-1-ylmethyl-1-(4-pyrrolidin-1-ylmethyl-phenyl)-piperidine;
4-{2-{1-(4-Piperidin-1-ylmethyl-phenyl)-pyrrolidin-3-yl}-ethyl}-morpholine;
Cyclohexyl-{1-(4-pyrrolidin-1-ylmethyl-phenyl)-piperidin-4-ylmethyl}-
amine;
Diethyl-{1-(4-pyrrolidin-1-ylmethyl-phenyl)-piperidin-4-ylmethyl}-amine;
30 Diethyl-{2-{1-(4-piperidin-1-ylmethyl-phenyl)-pyrrolidin-3-yl}-ethyl}-amine;
and
1-(2-Methyl-4-pyrrolidin-1-ylmethyl-phenyl)-4-pyrrolidin-1-ylmethyl-
pyrrolidine.

54. A pharmaceutical composition, comprising a compound of claim 1 and a pharmaceutically-acceptable excipient.
- 5 55. A compound of claim 1 isotopically-labelled to be detectable by PET or SPECT.
56. A method of inhibiting histamine H₃ receptor activity in a subject, comprising administering an effective amount of a compound of claim 1
10 to a subject in need of such inhibition of histamine H₃ receptor activity.
57. A method of treating a subject having a disease or condition modulated by histamine H₃ receptor activity, comprising administering to the subject a therapeutically effective amount of a compound of claim 1.
15
58. A method of claim 57, wherein said disease or condition is selected from the group consisting of sleep/wake disorders, arousal/vigilance disorders, migraine, asthma, dementia, mild cognitive impairment (pre-dementia), Alzheimer's disease, epilepsy, narcolepsy, eating disorders,
20 motion sickness, vertigo, attention deficit hyperactivity disorders, learning disorders, memory retention disorders, schizophrenia, nasal congestion, allergic rhinitis, and upper airway allergic response.
59. A method for treating a disease or condition modulated by at least one
25 receptor selected from the histamine H₁ receptor and the histamine H₃ receptor, said method comprising (a) administering to a subject a jointly effective amount of a histamine H₁ receptor antagonist compound, and (b) administering to the subject a jointly effective amount of a compound of claim 1, said method providing a jointly therapeutically effective
30 amount of said compounds.
60. The method of claim 59 wherein the histamine H₁ receptor antagonist and the compound of claim 1 are present in the same dosage form.

61. A method for treating diseases or conditions modulated by at least one receptor selected from the histamine H₂ receptor and the histamine H₃ receptor in a subject, comprising (a) administering to the subject a jointly effective amount of a histamine H₂ receptor antagonist compound, and
5 (b) administering to the subject a jointly effective amount of a compound of claim 1, said method providing a jointly therapeutically effective amount of said compounds.
- 10 62. The method of claim 39 wherein the histamine H₂ receptor antagonist and the compound of claim 1 are present in the same dosage form.
63. A method for treating one or more disorders or conditions selected from the group consisting of sleep/wake disorders, narcolepsy, and
15 arousal/vigilance disorders, comprising administering to a subject a therapeutically effective amount of a compound of claim 1.
64. A method for treating attention deficit hyperactivity disorders (ADHD), comprising administering to a subject a therapeutically effective amount
20 of a compound of claim 1.
65. A method for treating one or more disorders or conditions selected from the group consisting of dementia, mild cognitive impairment (pre-dementia), cognitive dysfunction, schizophrenia, depression, manic
25 disorders, bipolar disorders, and learning and memory disorders, comprising administering to a subject a therapeutically effective amount of a compound of claim 1.
66. A method for treating or preventing upper airway allergic response, nasal congestion, or allergic rhinitis, comprising administering to a
30 subject a therapeutically effective amount of a compound of claim 1.

67. A method for studying disorders mediated by the histamine H₃ receptor, comprising using an ¹⁸F-labeled or ¹¹C-labeled compound of claim 1 as a positron emission tomography (PET) molecular probe.

5 68. A composition comprising a compound of formula (I):



wherein

L is a direct bond, or an optionally C₁₋₄alkyl substituted radical selected from the group consisting of C₁₋₄alkylene or C₃₋₄alkenylene wherein NR¹R² is attached to an sp³ hybridized carbon, C₃₋₄alkynylene wherein NR¹R² is attached to an sp³ hybridized carbon, C₂₋₄alkylidene wherein NR¹R² is attached to an sp³ hybridized carbon, aryloxy wherein NR¹R² is not attached to the oxygen, arylthio wherein NR¹R² is not attached to the sulfur, C₂₋₄alkoxy wherein NR¹R² is not attached to the oxygen or a carbon attached to the oxygen, C₂₋₄alkylthio wherein NR¹R² is not attached to the sulfur or a carbon attached to the sulfur, and -C₂₋₃alkyl-X-C₁₋₂alkyl- wherein X is O, S or NH and wherein NR¹R² is not attached to a carbon attached to X;

p is 0, 1 or 2;

q is 1 or 2; provided that 2 ≤ p+q ≤ 4;

R¹ and R² are independently selected from hydrogen, C₁₋₃ alkyl, allyl, C₃₋₈ cycloalkyl, 5-9 membered heterocyclyl, phenyl, and (phenyl)C₁₋₃ alkylene, or taken together with the nitrogen to which they are attached, they form a non-aromatic 4-13 membered heterocyclyl optionally including up to two additional heteroatoms independently selected from O, S, and NH; and wherein R¹ and R² are optionally and independently substituted with substituents

selected from the group consisting of trifluoromethyl, halo, nitro, cyano, hydroxy, and C₁₋₃ alkyl;

one of R³, R⁴ and R⁵ is G and the other two independently are hydrogen, fluoro, chloro, bromo, nitro, trifluoromethyl, methyl, or C₁₋₃ alkoxy ;

G is L²Q;

L² is unbranched -(CH₂)_n- wherein n is an integer from 1 to 7;

Q is NR⁸R⁹ wherein R⁸ is independently selected from hydrogen, C₁₋₆ alkyl, C₃₋₆ alkenyl, C₄₋₉ carbocyclyl, 3-12 membered heterocyclyl, phenyl, (5-9-membered heterocyclyl)C₁₋₆ alkylene, and (phenyl)C₁₋₆ alkylene; and R⁹ is independently selected from C₁₋₆ alkyl, C₃₋₆ alkenyl, C₄₋₉ membered carbocyclyl, 3-12 membered heterocyclyl, phenyl, (5-9-membered heterocyclyl)C₁₋₆ alkylene, and (phenyl)C₁₋₆ alkylene; or Q is a saturated 3-15 membered N-linked heterocyclyl, wherein, in addition to the N-linking nitrogen, the 3-15 membered heterocyclyl may optionally contain between 1 and 4 additional heteroatoms independently selected from O, S, and NH;

and wherein Q is optionally substituted with 1-3 substituents selected (in addition to the preceding paragraph) from the group consisting of *tert*-butyloxycarbonyl, hydroxy, halo, nitro, amino, cyano, carboxamide, C₁₋₆ alkyl, C₁₋₆ acyl, 5-9-membered heterocyclyl, -N(C₁₋₆ alkyl)(5-9 membered heterocyclyl), -NH(5-9 membered heterocyclyl), -O(5-9 membered heterocyclyl), (5-9 membered heterocyclyl)C₁₋₃ alkylene, C₁₋₂-hydroxyalkylene, C₁₋₆ alkoxy, (C₃₋₆ cycloalkyl)-O-, phenyl, (phenyl)C₁₋₃ alkylene, and (phenyl)C₁₋₃ alkylene-O-; and where said substituent groups of Q may optionally have between 1 and 3 substituents independently selected from trifluoromethyl, halo, nitro, cyano, hydroxy, and C₁₋₃ alkyl;

R^a are independently C₁₋₃ alkyl, trifluoromethyl; and m is 0, 1, 2 or 3;

or a pharmaceutically acceptable salt, ester, tautomer, solvate or amide thereof.